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MESSAGE:

Re: Serial No. 09/730,790

As you requested, attached is a "Brief Description of the Drawings" relating to the subject application.

If you have any questions, please contact me.

Thank you.

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BRIEF DESCRIPTION OF THE DRAWINGS

[Figure 1: NGF-Secreting and Control Grafts Within the Intermediate Component of the Ch4 region.

(A) p75-immunolabeled coronal section of the intermediate component of Ch4 showing an NGF-secreting cell graft. The graft is penetrated by cholinergic axons. **(B)** Thionin-stained section taken adjacent to that in (A) identifies graft boundaries within the Ch4 region. **(C,D)** Comparable p75-immunolabeled and thionin-stained sections from a control aged monkey that received ß-gal expressing fibroblasts. Graft survival is comparable to that of NGF grafts, but fewer axons penetrated the grafts. Scale bar = 1 mm.

Figure 2: Quantification of Cholinergic Innervation Densities.

Cholinergic axon density was determined in multiple cortical regions. Quantified regions included inferior temporal cortex layers II **(IT-II)** and V **(IT-V)**; Insular cortex layers II **(INS-II)** and V **(INS-V)**; cingulate cortex layer II **(CING)**; frontal cortex layer II **(FR)**; and hippocampal formation, stratum radiatum of CA1 **(HF)**. Axon densities were determined by superimposing a 6 X 6 grid over a highly magnified image captured from one of the defined regions (see inset). All AChE-stained fibers crossing the gridlines (arrows in inset) were counted to yield an index of innervation density. Scale bar = 5 mm. Bar in inset = 35 µm.

Figure 3: Age-Related Decline in Mean Cortical Cholinergic Innervation is Reversed by NGF Gene Delivery to Cholinergic Somata in the Basal Forebrain.

AChE staining in the insular cortex of young, aged-control, and aged-NGF-grafted rhesus monkeys. **(A)** The normal density of cholinergic axons is illustrated in young subjects. **(B)** Axon density is reduced in aged, control-grafted subjects. **(C)** AChE-stained fiber density is significantly increased in aged monkeys that received grafts of autologous NGF-secreting fibroblasts into the intermediate division of Ch4. Scale bar A - C = 35 µm. **(D)]** --Figure 1:-- Quantification of cholinergic axon density. To compare cholinergic innervation densities across multiple cortical regions, normalized z-scores of density measurements from each cortical region were calculated and then averaged. A significant overall group effect was present by one way ANOVA ($p < 0.0001$). Aging was associated with a significant reduction in overall cholinergic fiber density (* $p < 0.0001$, Post hoc Fischer's), and this was restored in recipients of NGF-secreting cells. Black bars, young

monkeys; red bars, aged-controls; blue bars, aged-NGF-grafted subjects. Error bars represent standard errors of the mean.

[Figure 4:] --Figure 2:-- Changes in Cholinergic Axon Density Across Cortical Regions.

Control-aged monkeys (red bars) exhibit a significant decline in cortical cholinergic innervation compared to young intact animals (black bars) in most cortical regions. Aged recipients of NGF-secreting grafts (blue bars) exhibit a significant reversal of age-related loss in cholinergic innervation; however, this effect is significant only in cortical regions (insula and inferior temporal cortex) innervated primarily by cholinergic neurons of the intermediate division of Ch4, which was targeted for grafting. Numbers in parentheses below each cortical region indicate p value for ANOVA.

LEGEND TO FIGURES 1-[4:] --2:--

* - significantly reduced compared to young animals ($p < 0.05$, Post hoc Fischer's);

[# - significantly increased compared to aged control animals ($p < 0.05$, Post hoc Fischer's). INS: insular cortex; IT: inferior temporal cortex; CING: cingulate cortex; FR: frontal cortex; HF: hippocampal formation.

Figure 5:

Reprint of the nucleotide sequence coding for human beta nerve growth factor as shown in GENBANK Accession No. X52599.

Figure 6:

Reprint of the nucleotide sequence coding for human NT-3 as shown in GENBANK Accession No. E07844.]

Per Amendment of April 14, 2001

BRIEF DESCRIPTION OF THE DRAWINGS

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LEGEND TO FIGURES 1-2:

* - significantly reduced compared to young animals ($p < 0.05$, Post hoc Fischer's);